

## Conversion of Atrial Fibrillation and Flutter by Propranolol

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Propranolol, a synthetic derivative of isoprenaline, was developed as a beta adrenergic blocking agent (Black *et al.*, 1964). It has also been shown to have anti-arrhythmic properties (Stock and Dale, 1963; Wolfson, Robbins, and Krasnow, 1966). These effects, however, appear to derive from characteristics other than beta adrenergic blockade. Vaughan Williams has shown that the changes induced by propranolol upon muscle action potentials are identical with those of quinidine (Morales-Aguilera and Vaughan Williams, 1965). This resemblance is supported by the ability of propranolol to abolish ventricular premature contractions or to protect against ventricular fibrillation in reserpinized animals (Aroesty and Cohen, 1966; Wolfson *et al.* 1966). Although not an adrenergic blocker, the dextro-isomer of propranolol also depresses ventricular irritability (Lucchesi, 1965).

Thus far, there have been few data reported suggesting a 'quinidine-like' effect upon the atria. Harrison, Griffin, and Fiene (1965) included in their series one subject with atrial flutter converted to a sinus mechanism by propranolol. With respect to atrial fibrillation, however, Besterman and Friedlander (1965) correctly concluded that, 'there is no evidence that propranolol is of any value' for the restoration of sinus rhythm. There has been one previous report of successful conversion of atrial fibrillation with propranolol and quinidine in combination (Stern, 1966). Quinidine had either failed to change the rhythm when used alone, or had produced symptoms of toxicity.

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### PATIENTS AND METHODS

Three patients were given propranolol\* to slow the ventricular response to atrial fibrillation. Surprisingly, the rhythm was converted to normal sinus. All three had been treated unsuccessfully with digitalis; two were refractory to DC countershock; and one had been uncontrolled by quinidine. In addition, two patients with atrial flutter transiently maintained a sinus mechanism after treatment with propranolol.

*Case 1* (Fig. 1). A 59-year old man underwent open-heart surgery for débridement of a calcified, stenotic, bicuspid aortic valve. Two days after operation he abruptly developed atrial fibrillation for the first time. The ventricular response averaged 180/min. All serum electrolytes and blood gases were within normal limits. He was febrile, with scattered râles clearing on cough, and wheezes controlled with an aminophylline drip. A directly recorded mean arterial pressure was 80 mm. Hg. Medication included digoxin 0.125 mg. intramuscularly daily. Over the next 14 hours, 2 unsuccessful attempts at conversion by DC countershock were made, and, in addition, he received a total of 0.5 mg. ouabain and 0.5 mg. digoxin in divided intravenous doses. The only result was to slow his ventricular response from an average rate of 180/min. to 160/min., with intermittent regularization of the rhythm (nodal tachycardia), suggesting digitalis intoxication. At this point he was given five 2 mg. infusions of propranolol at 20-minute intervals, producing a sinus rhythm which relapsed into atrial fibrillation within 15 minutes on four separate occasions. His clinical state was unchanged, with a mean blood pressure of 80, clear lung fields, and adequate urine output. Propranolol, 4 mg., was then given intravenously in a single dose, followed by an additional 3 mg. in 15 minutes. One hour later, he was in normal sinus rhythm, with a mean blood pressure of 85 mm. Hg. He was placed on quinidine 0.2 g. intramuscularly 4 times a day and ouabain 0.1 mg. intravenously 4 times a day.

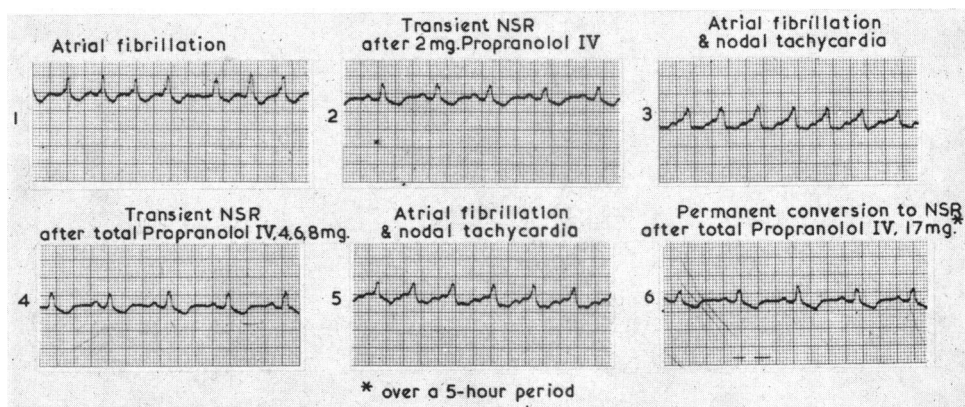


FIG. 1.—Case 1. Electrocardiogram (lead II) shows repeated conversion of atrial fibrillation to sinus rhythm with propranolol. See case report for details.

Within 24 hours, however, he reverted to atrial fibrillation once more. The ventricular rate was 160/min. His condition in every other respect was unchanged. DC countershock was again unsuccessful, and attended by considerable ventricular irritability. Propranolol, 5 mg. intravenously, again converted the rhythm to normal sinus within 5 minutes. Propranolol, 2 mg. intravenously every 4 hours, was added to his regimen.

Two days later, still in normal sinus rhythm, he was given propranolol 20 mg. orally every 6 hours. After 2 days on this programme he once again reverted to atrial fibrillation with a rapid ventricular rate. Five minutes after receiving 5 mg. propranolol intravenously, he was back in normal sinus rhythm and has since been maintained with a larger dose of propranolol, 40 mg. orally 4 times a day.

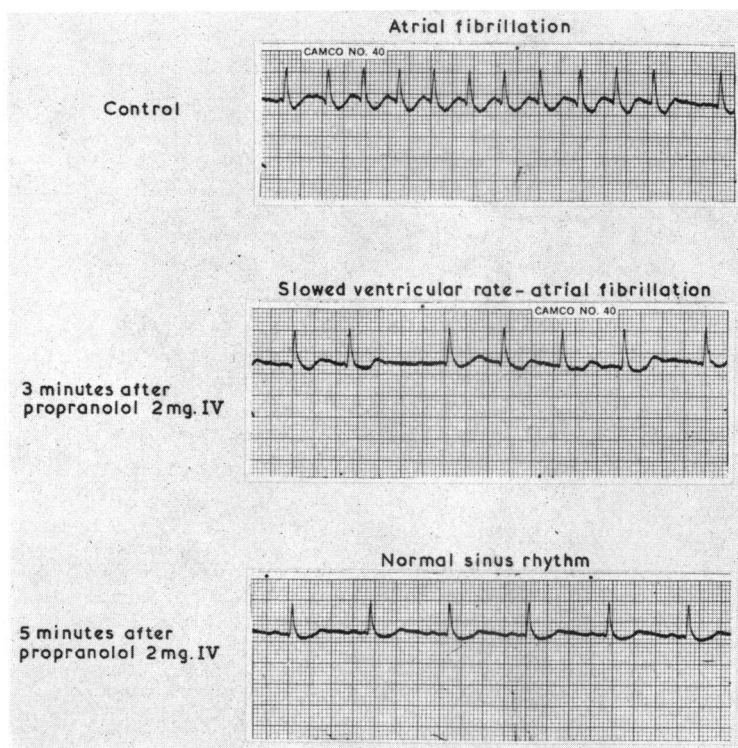


FIG. 2.—Case 2. Electrocardiogram (lead II), shows slowing of atrial fibrillation with subsequent conversion to sinus rhythm. See case report for details.

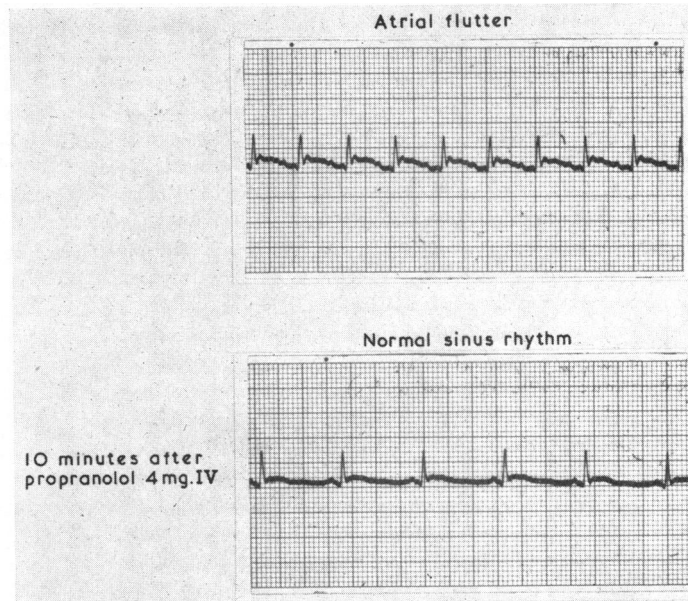


FIG. 3.—Case 4. Electrocardiogram (lead II), 1 week after internal mammary implant surgery, shows atrial flutter with 2:1 block was converted transiently to sinus rhythm.

*Case 2* (Fig. 2). A 60-year-old man, with a 3-year history of severe angina pectoris, had noted improvement in his symptoms while taking propranolol, 40 mg. 6 times daily. He underwent internal mammary artery pedicle implantation to the antero-lateral surface of his left ventricle. Propranolol had been withdrawn. Three days later he had severe anginal pain and was found to be in atrial fibrillation with a ventricular rate of 170. Over the next 30 minutes his rhythm was predominantly atrial fibrillation, alternating with periods of sinus rhythm. Upon receiving ouabain, 0.1 mg. intravenously, he reverted to normal sinus rhythm only to return to atrial fibrillation with a ventricular rate of 180 within 10 minutes. All electrolytes were normal. At this point, propranolol, 2 mg., was administered intravenously. Two minutes later, the ventricular rate was 100, and at 5 minutes the rhythm was normal sinus at 75/minute.

He was placed on propranolol, 40 mg. every 4 hours, and subsequently discharged on this medication without recurrence of arrhythmia.

*Case 3.* This 56-year-old woman, with rheumatic aortic stenosis and insufficiency, underwent valve replacement. Three days later, the abrupt onset of atrial fibrillation at a ventricular rate of 180 was noted. The only electrolyte abnormality present was a serum potassium level of 5.6 mEq/l. A total of 0.5 mg. ouabain was given intravenously in divided doses over a period of 2½ hours. This slowed the ventricular rate only to 160/min. Cardioversion changed the rhythm to an atrial tachycardia with 2:1 block and an atrial rate of 240. This reverted to atrial fibrillation within one hour. Given an initial infusion of 2 mg. propranolol,

followed by an additional 3 mg. within 15 minutes, the ventricular rate slowed from 160 to 90. The patient was then given an oral dose of 40 mg. propranolol. Four hours later, she was found to be in normal sinus rhythm with a rate of 105/min.

*Case 4* (Fig. 3). A 41-year-old man had had severe angina pectoris for about 6 months. Propranolol had produced a significant remission of his symptoms. The drug was discontinued prior to an internal mammary artery implantation. Two days after the operation, atrial flutter (atrial rate 300) with 2:1 block was noted, associated with a fall in blood pressure to 90/80 mm. Hg. He was afebrile, with normal electrolytes and blood gases. Given 4.0 mg. propranolol, he converted to normal sinus rhythm within 5 minutes. One hour later, he returned to atrial flutter. Propranolol, 5 mg., did not affect the rhythm at this time. No attempt was made to use the drug more vigorously.

Over the next 3 days, it became apparent that the patient had suffered a fresh anterior wall myocardial infarction. He received large doses of oral and intravenous digitalis glycosides during this period, finally resulting in a stable sinus mechanism one week after operation.

*Case 5* (Fig. 4). This 43-year-old man with three-vessel coronary artery disease and hypercholesterolemia had an internal mammary pedicle implanted into the left ventricular surface. Eight days after operation his cardiac rhythm abruptly changed from normal sinus to atrial flutter with 2:1 block and ventricular rate of 150. Serum electrolytes were within normal limits at the time. He was receiving digoxin, 0.25 mg. orally twice a day.

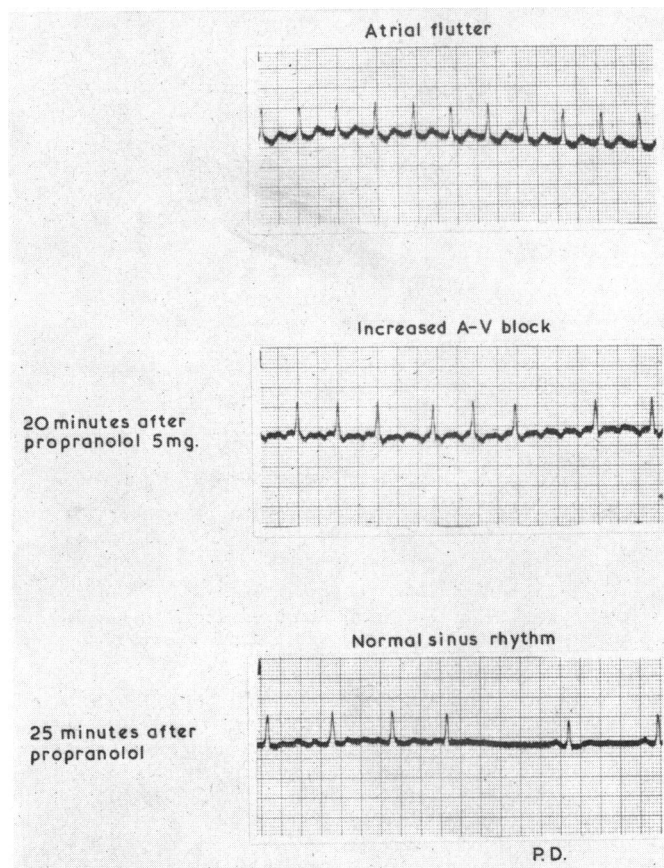


FIG. 4.—Case 5. Electrocardiogram (lead II), 13 days after mammary implant, shows atrial flutter with 2:1 block converted to sinus rhythm. Note transient atrial fibrillation supervening before conversion to sinus mechanism.

Blood pressure fell from a normal range of 130/80 to 106/80 mm. Hg. Given propranolol, 5 mg. intravenously, he first developed 3:1 A-V block and then abruptly converted to normal sinus rhythm 20 minutes after the propranolol infusion. Immediately before conversion, his atrial rate accelerated and became irregular (Fig. 4). Atrial arrest ensued, followed by a normal sinus mechanism. After conversion, blood pressure was 98/80 mm.Hg, subsequently rising to 130/80 mm. Hg. He was placed on propranolol, 40 mg. orally, every 6 hours. However, after each dose, blood pressure declined to 100/75 mm. Hg. The amount of propranolol given to this patient was decreased to 20 mg. orally every 6 hours, then to 20 mg. every 8 hours, and then discontinued after 6 days as cardiac rhythm remained normal.

One day later, atrial flutter recurred. This time 5 mg. propranolol, intravenously, reverted the arrhythmia only when the systemic blood pressure was simultaneously raised to 170/110 mm. Hg by intravenous phenylephrine. The conversion lasted for 2 hours only,

after which atrial flutter was re-established, and was now refractory to 2 infusions of propranolol (5 mg.) over a 20-minute period. Over the next 2 days, accelerated digitalis administration resulted in permanent conversion to normal sinus rhythm. He has since been treated with oral propranolol (as therapy for angina pectoris), without side-effect.

#### COMMENT

All five patients mentioned in this report were studied during the immediate post-operative period. Arrhythmias occurring under these circumstances are, certainly, frequently labile. On the other hand, their reversion is often difficult to accomplish or maintain. Countershock is notoriously ineffective in these respects.

The use of propranolol for its 'quinidine-like' effect should be considered. It may result in rapid reversion of atrial fibrillation or flutter. Even if

conversion does not result, the ventricular response to atrial fibrillation is invariably slowed, even when digitalis has had no effect upon the A-V node. Atrial flutter will usually respond in like manner.

Significantly, propranolol is among the safest anti-arrhythmic drugs currently available. Its use should be avoided in the presence of bradycardia or pathological A-V block, severe pulmonary hypertension, and advanced congestive heart failure (unless caused by arrhythmia). Bronchospasm may be exacerbated by propranolol, but this effect can be overcome by theophylline and its derivatives. In the absence of these absolute and relative contraindications, however, the use of propranolol has not been attended by serious side-effects. The same cannot be said of quinidine, for example (Selzer and Wray, 1964).

#### SUMMARY

Three cases of atrial fibrillation and two of atrial flutter, all of recent origin, have been converted to sinus rhythm by propranolol. Digitalis, quinidine, and DC countershock had been completely ineffective in three of the five cases. Propranolol may offer a safe and effective approach to this problem.

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